Results of the Voluntary Harmonisation Procedure 2009 – 2018

HMAs Clinical Trials Facilitation Group

Status 1.1.2019
The graph depicts evaluable Voluntary Harmonisation Procedures excluding 11 procedures from the pandemic influenza situation in 2009.
2013 to 2018
16-23% of all multinational clinical trials in Europe underwent a VHP before they were submitted to the National competent authorities
Percentages of VHP decisions from 3/2009 to 1.2.2019

- Positive: 75.7%
- Open: 2.5%
- Negative and finally neg. not fulfilling condition: 5.7%
- Rejected due to inability to find a REF-NCA in initial VHP and SR-VHP*: 6.4%
- Divergent opinions: 4.0%
- Withdrawn by applicant: 5.6%

*rejection to participate in 2nd waves (SR-VHP (21) and case s, where no REF-NCA (70) was found.
Distribution of commercial / non-com. Sponsors in VHP

- Commercial: 91.4%
- Non-commercial: 8.6%
### Distribution of regions/countries of VHP sponsors

<table>
<thead>
<tr>
<th>Country of Sponsor</th>
<th>Number of Voluntary Harmonisation Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States of America</td>
<td>551</td>
</tr>
<tr>
<td>SWITZERLAND</td>
<td>222</td>
</tr>
<tr>
<td>Germany</td>
<td>188</td>
</tr>
<tr>
<td>UNITED KINGDOM</td>
<td>97</td>
</tr>
<tr>
<td>FRANCE</td>
<td>90</td>
</tr>
<tr>
<td>DENMARK</td>
<td>64</td>
</tr>
<tr>
<td>BELGIUM</td>
<td>56</td>
</tr>
<tr>
<td>SWEDEN</td>
<td>34</td>
</tr>
<tr>
<td>SPAIN</td>
<td>18</td>
</tr>
<tr>
<td>ITALY</td>
<td>11</td>
</tr>
<tr>
<td>AUSTRIA</td>
<td>13</td>
</tr>
<tr>
<td>NETHERLANDS</td>
<td>13</td>
</tr>
<tr>
<td>IRELAND</td>
<td>14</td>
</tr>
<tr>
<td>CANADA</td>
<td>11</td>
</tr>
<tr>
<td>JAPAN</td>
<td>7</td>
</tr>
<tr>
<td>ISRAEL</td>
<td>5</td>
</tr>
<tr>
<td>AUSTRALIA</td>
<td>4</td>
</tr>
<tr>
<td>CZECH REPUBLIC</td>
<td>6</td>
</tr>
<tr>
<td>SINGAPORE</td>
<td>3</td>
</tr>
<tr>
<td>LUXEMBOURG</td>
<td>2</td>
</tr>
<tr>
<td>Portugal, Taiwan, Ukraine, Iceland</td>
<td>1</td>
</tr>
</tbody>
</table>

The total number of different sponsors is **330**

25 sponsors use VHP often >10-100 times

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CTFG: Results of the Voluntary Harmonisation Procedure 2009 –2018
Member States joining the VHP

<table>
<thead>
<tr>
<th>mean of Member States per Voluntary Harmonisation Procedure (Without SR-VHP) n=1243</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>min</td>
<td>2</td>
</tr>
<tr>
<td>max</td>
<td>22</td>
</tr>
</tbody>
</table>
## Distribution of IMPs

### 1.2.2019

<table>
<thead>
<tr>
<th>Group IMP</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemicals</td>
<td>51,0</td>
</tr>
<tr>
<td>Biologicals</td>
<td>49,0</td>
</tr>
</tbody>
</table>

CTFG: Results of the Voluntary Harmonisation Procedure 2009 –2018
Distribution of VHPs by phase of the clinical trial

Status 1.1.2019

- Phase I: 5.4%
- Phase II: 31.7%
- Phase III: 57.3%
- Phase IV: 4.1%
- FIH: 1.5%
## Status of the IMP

Status 1.1.2019

<table>
<thead>
<tr>
<th>Status marketing authorisation</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>authorised</td>
<td>19%</td>
</tr>
<tr>
<td>non-authorised</td>
<td>81%</td>
</tr>
</tbody>
</table>
Numbers of VHP-Substantial Amendments
2009 – 1.1.2019

CTFG: Results of the Voluntary Harmonisation Procedure 2009 – 2018
Percentages of VHP SA decisions from 3/2009 to 01.02.2019

- Positive: 88.9%
- Divergent opinions: 1.8%
- Negative*: 7.0%
- Withdrawn: 2.3%

* Some cases, where the REF-NCA was lost and no replacement found.
Number of VHP as REF-NCA per NCA 2015-2018
Priority i.e. Number of VHPs divided by REF-NCA- ships of the last 365 days

(e.g. Denmark was the REF-NCA in 33.3% of the VHPs, in which it participated)

6.2.2018 – 5.2.2019

[Bar chart showing priority numbers for different countries from 6.2.2018 to 5.2.2019]
% sponsor proposal in **nominated** VHPs of the last 365 days
e.g. Denmark was proposed by sponsors in 21,6% of VHPs in which it participated

status 5.2.2019
Rejections due to lack of REF-NCA

DETERMINED BY CTFG-ALGORITHM PRIORITY AND NOT BY SPONSOR NOMINATION

I.E.

NEITHER THE SPONSORS PROPOSAL, NOR THE MEMBER STATE WITH THE HIGHEST PRIORITY NOR ANY OTHER OF THE P-NCA VOLUNTEERED
rejections due to lack of REF-NCA

- 2015: 218 all VHP, 3 rejected VHPs
- 2016: 209 all VHP, 31 rejected VHPs
- 2017: 191 all VHP, 22 rejected VHPs
- 2018: 199 all VHP, 14 rejected VHPs
% rejections due to lack of REF-NCA

N.B. A proactive measure to avoid rejections was introduced late 2017 and works
No of rejected VHP due to lack of ref-NCA

2015-2018

BELGIUM: 3
BULGARIA: 7
ESTONIA: 1
FINLAND: 2
FRANCE: 19
Germany BfArM: 6
GREECE: 6
ITALY: 1
LATVIA: 2
NETHERLANDS: 11
NORWAY: 1
POLAND: 2
ROMANIA: 7
SPAIN: 7
SWEDEN: 1
questions / comments can be sent via mail to

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